

What is claimed is:

1. A cell culture comprising host cells having their genome manipulated to:
 - a) express a chemical or biological molecule useful in a therapeutic composition;

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- b) not express a PrP protein due to the alteration of any endogenous PrP sequences.

2. The cell culture of claim 1 wherein the endogenous PrP gene is ablated.

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3. The cell culture of claim 2, wherein the genome of the host cell is further altered to express an exogenous PrP gene, which gene expression enhances viability of the cell.

- 15 4. The cell culture of claim 3, wherein the exogenous PrP gene is from a species genetically diverse from the host cell, and wherein the genetically diverse exogenous PrP gene renders the host cell resistant to prion infection by the PrP^{Sc} form of the host cell species.

5. The cell culture of claim 4, wherein:

- 20 a) the host cells are primate cells; and
- b) the genetically diverse exogenous gene is from a species selected from the group consisting of: mouse, hamster, and rat.

6. The cell culture of claim 4, wherein:

- 25 a) the host cells are from a species selected from the group consisting of horse, cow, sheep, dog and cat; and
- b) the genetically diverse exogenous PrP gene is selected from the group consisting of: mouse, hamster, or rat.

7. The cell culture of claim 4, wherein the exogenous PrP gene genetically diverse from the host cell is operably linked to an inducible promoter.

8. The cell culture of claim 1, wherein the host cells are hybridoma cells.

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9. A method for producing a therapeutic composition free from infectious prion contamination comprising:

- a) ablating an endogenous PrP gene in a mammalian somatic host cells;
- b) producing a therapeutic composition in said host cells; and
- c) isolating said therapeutic composition from said host cells;

10 wherein the isolated therapeutic composition is characterized by an inability to transmit a prion-mediated pathology to a subject of the same species as the host cells.

15 10. The method of claim 9, wherein the therapeutic composition is for human use.

11. The method of claim 9, wherein the therapeutic is for bovine, equine, canine, feline or ovine use.

20 12. The method of claim 9, wherein the therapeutic composition is selected from the group consisting of: a peptide, a protein, an antisense molecule, a ribozyme, a viral vector, an expression vector, and a plasmid.

13. A method for producing a therapeutic composition free from infectious prion contamination comprising:

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- a) ablating an endogenous PrP gene in a host cell;
- b) introducing exogenous PrP sequences from a species genetically diverse from said host cell into said host cell;
- c) expressing said exogenous PrP sequences;

d) manipulating the genome of the cell to produce a therapeutic composition from said host cell; and

e) isolating said therapeutic composition from said host cell;

wherein the expression of the exogenous PrP sequences allows necessary expression of

5 PrP and wherein the isolated therapeutic composition cannot transmit a prion-mediated pathology to a subject of the same species as the host cell.

14. The method of claim 13, wherein the exogenous PrP gene is operatively fused to an inducible promoter.

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15. The method of claim 13, wherein the therapeutic composition is for human use.

16. The method of claim 13, wherein the therapeutic composition is for bovine, equine, porcine, canine, feline or ovine use.

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17. The method of claim 13, wherein the therapeutic composition is selected from the group consisting of: a peptide, a protein, an antisense molecule, a ribozyme, a viral vector, an expression vector, and a plasmid.

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18. A method for producing a therapeutic composition free from infectious prion contamination comprising:

a) ablating the endogenous PrP gene in a somatic host cell;

b) introducing exogenous PrP sequences from a genetically similar species, said exogenous sequences operably linked to an inducible promoter;

c) suppressing expression of the exogenous PrP sequences;

d) producing a therapeutic composition in said host cell; and

e) isolating the therapeutic composition from said host cell;

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wherein the isolated therapeutic composition produced during suppression of PrP expression cannot transmit a prion-mediated pathology to a subject of the same species as the host cell.

5 19. The method of claim 18, wherein the therapeutic composition is for human treatment.

20. The method of claim 18, wherein the therapeutic composition is for bovine, equine, porcine, canine, feline or ovine treatment.

10 21. The method of claim 18, wherein the therapeutic composition is selected from the group consisting of: a peptide, a protein, an antisense molecule, a ribozyme, a viral vector, an expression vector, and a plasmid.

15 22. An isolated therapeutic composition is characterized by an inability to transmit a prion-mediated pathology to a subject of the same species as the host cells.

23. The composition of claim 22, wherein the composition is produced using the method of claim 9.

20 24. The composition of claim 22, wherein the composition is produced using the method of claim 13.

25 25. The composition of claim 22, wherein the composition is produced using the method of claim 18.

26. The isolated composition of claim 22, wherein the therapeutic composition is for human use.

27. The isolated composition of claim 22, wherein the therapeutic composition is for bovine, equine, canine, feline or ovine use.

28. The isolated composition of claim 22, wherein the therapeutic composition is comprised of a peptide, a protein, an antisense molecule, a ribozyme, a viral vector, an expression vector, and a plasmid.

29. A method of producing antibodies free from infectious prion contamination comprising:

- 10 a) inoculating a mammal with an antigen to produce antibodies specific to said antigen;
- b) fusing isolated B lymphocytes expressing said antibodies to a mammalian cell line to establish a hybridoma line which expresses said antibodies;
- c) producing said antibodies; and
- 15 d) isolating said antibodies;

wherein the hybridoma line has an altered endogenous PrP gene and said isolated antibodies cannot transmit a prion-mediated pathology to a subject of the same species as the host cell.

20 30. The method of claim 29, wherein the endogenous PrP gene is altered prior to the establishment of the hybridoma line.

31. The method of claim 29, wherein the endogenous PrP gene is altered in the B lymphocytes and the mammalian cell line prior to the establishment of the hybridoma line.

25 32. The method of claim 29, wherein the hybridoma is further altered to express exogenous PrP sequences.

33. The method of claim 29, wherein the expression of the exogenous PrP sequences is operably linked to an inducible promoter that can suppress expression of PrP during antibody production.

5 34. A method for producing humanized antibodies free from infectious prion contamination comprising:

- a) introducing an expression vector comprised of sequences encoding an antibody into a primate cell line with an altered endogenous PrP gene;
- b) producing said antibodies by induction of said expression vector; and
- c) isolating said antibodies;

10 wherein the isolated antibodies are free from infectious primate prions and cannot transmit prion-mediated disease to primate subjects receiving said isolated antibodies.

15 35. The method of claim 34, wherein the primate cell line has an ablated endogenous PrP gene.

36. The method of claim 34, wherein the primate cell line is further altered to express an exogenous PrP gene.

20 37. The method of claim 34, wherein the expression of the exogenous PrP sequence is operably linked to an inducible promoter that can suppress expression of PrP during antibody production.

25 38. An isolated antibody characterized by an inability to transmit a prion-mediated pathology to a subject of the same species as the host cells.

39. The antibody of claim 38, wherein the antibody is produced using the method of claim 29.

40. The antibody of claim 38, wherein the antibody is produced using the method of claim 34.

41. The isolated antibody of claim 38, wherein the antibody is for human
5 therapeutic use.

42. The isolated antibody of claim 38, wherein the antibody is for bovine, equine,
porcine, canine, feline or ovine therapeutic use.